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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,136	06/07/2001	Michael G. Walker	PB-0003 USN	5258

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EXAMINER	
MOORE, WILLIAM W 13	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,136	WALKER ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2, 4-10 and 12-15* is/are pending in the application.

4a) Of the above claim(s) *9,10 and 12-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *12-15* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

Applicant's cancellation of claims 1, 3 and 11 and submission of amendments to claims 2, 4, 7 and 8 with Amendment B, Paper No. 12 filed December 10, 2002, removes the subject matter telephonically elected with traverse for prosecution on July 7, 2002, from the rejections of record of claims 1 and 3 herein under 35 U.S.C. §102(b) over prior art of record. While not styled as such, the Declaration of the co-inventor, Dr. Michael G. Walker, Paper No. 11 filed December 10, 2002, is considered a Declaration under 37 CFR 1.132 and is discussed hereinbelow. While the amendments of Paper No. 12 to claims 7 and 8 present no issues, both the amendment to clause (d) of claim 2 and the amendment that adds clause (c) to claim 4 raise the issue of new matter.

The amendment filed December 10, 2002, is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: (a) that portion of the subject matter described by clause (d) of claim 2 which is a naturally-occurring variant of a polynucleotide having at least 95% identity to an isocoding, or isocomplementary, polynucleotide of clauses (b) and (c) of claim 2, and (b) the subject matter described clause (c) of claim 4. Although Applicant suggests - at page 3 of Paper No. 12 - that support for the amendments of both claims 2 and 4 is found at page 3, lines 27-33, of the specification, the referenced text of the specification provides no support for a specific amount of 5% divergence in the coding capacity of a polynucleotide otherwise isocoding, or isocomplementary, to a nucleotide sequence of SEQ IDs NOs:1-5. Instead, the only reference to a value of "95% sequence identity" occurs at page 8, lines 8-10, of the specification and it concerns only divergence from a disclosed nucleic acid sequence of an

"NSEQ" where "NSEQ" is defined at page 3 of the specification as SEQ IDs NOs:1-5. Since isocoding, or isocomplementary, nucleic acid sequences of clauses (b) and (c) of claim 2 need only have 66.66% identity with one of the disclosed nucleic acid sequences of SEQ IDs NOs:1-5 where only the third codon positions are altered, the additional degree of divergence permits 63.33% identity, which degree of identity is not indicated anywhere in the specification. Similarly, there is no support anywhere in the specification for a specific amount of 5% divergence in amino sequences of variants of the polypeptide that has the amino acid sequence of SEQ ID NO:6 or for any specific degree of amino acid sequence non-identity with SEQ ID NO:6. Applicant is required to cancel the new matter in the reply to this Office Action.

Election/Restrictions

Applicant's affirmation of an election with traverse of the subject matter of the nucleotide species of SEQ ID NO:4, and of its encoded polypeptide having the amino acid sequence of SEQ ID NO:6, in Paper No. 12 is acknowledged. One ground of traversal stated at page 4 of Paper No. 12 is that the inventions of Groups I and II are so closely related as to present no undue burden, but the amendment to claim 2 removes the invention of Group II from the claims, thus the restriction requirement as between the products of Groups I and II is moot where no non-specific, yet hybridizing, "probe" is described by any claim. Applicant makes no further argument traversing the restriction requirement of record as between the included method of use of Group I and the included method of use of Group II, represented by claim 10. Thus the requirement for restriction between the included methods of use of Groups I and II is still deemed proper and is therefore made FINAL. Applicant also makes no argument in traversal of the restriction requirement of record as between Group I and Groups III and IV, comprising the subject matters of claim 9, thus the requirement for restriction as between Group I and Groups III

and IV is still deemed proper and is therefore made FINAL. A second ground of traversal stated at page 4 of Paper No. 12 is that the inventions of the several polynucleotides having the nucleic acid sequences set forth in SEQ IDs NOs:1-5 "are sufficiently few in number to not constitute an undue [search] burden". This is not found persuasive because Applicant can point to no structural similarity between any of the nucleotide sequences that would permit a search for one to constitute a search for the others. Applicant cannot show that any two sequences are so linked as to form a single general inventive concept and a separate search for patentability over the prior art is an undue burden, thus the requirement for restriction among the separate nucleic acid sequence products of SEQ IDs NOs:1-5 is still deemed proper and is therefore made FINAL. This application contains claims 9 and 10 drawn to inventions elected without traverse in Paper No. 12.

Newly submitted claims 12-15 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: 35 U.S.C. §§121 and 372 require that inventions of the remaining elected claims 2 and 4-8 and of the new claims 12-15 share unity of invention. The invention of Group I and the invention of the new claims 12-15 are not so linked as to form a single general inventive concept because the polynucleotide product of Group I and its included method of use in making a purified polypeptide of Group I using the included expression vector and host cell, share no same or corresponding special technical feature with the new claims' composition comprising a "plurality of polynucleotides". This is because the invention of Group I needs no further component of the new claims' composition comprising a "plurality of polynucleotides" thus shares no technical feature which is special with the invention of the new claims and because a method of use of a polynucleotide of SEQ ID NO:4 in a method of making an encoded polypeptide in Group I is mutually exclusive with a method of its use in the new claims in detecting gene expression. Since applicant has received an action on the merits

for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 12-15 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 2 and 4-8 are therefore examined herein to the extent that they describe the invention of Group I which is a polynucleotide capable of encoding the amino acid sequence of SEQ ID NO:6, a polypeptide having the amino acid sequence of SEQ ID NO:6 and compositions comprising same, and a method of making a polypeptide having the amino acid sequence of SEQ ID NO:6 using expression vectors and host cells comprising the polynucleotide.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 4-8 are for reasons of record rejected under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. Applicant's arguments filed December12, 2002, have been fully considered but they are not persuasive, because they are incomplete where the Declaration under 37 CFR 1.132, Paper No. 11 filed is insufficient to overcome the rejection of claims 2 and 4-8 for lack of a patentable utility set forth in the last Office action and Applicant has not provided the journal article referenced in the Declaration, i.e., Thompson et al., **Genomics Research**, Vol. 12, pages 1517-1522, to support statements in paragraphs 4-5 and 7 of the Declaration, which has no paragraph 6. Certain observations are made herein to the extent that the Declaration's paragraph 7 addresses the specification's disclosure. First, It is noted that the arguments of Paper No. 12 and the statements in the Declaration posit no potential utility for subject matters of the broad genus of products described by clause (b), and in part by clause (c), of claim 2 and the even broader product genus described by

clause (d) of claim 2. Likewise, the arguments of Paper No. 12 and the statements in the Declaration posit no potential utility for subject matters of the broad genera of products described by clauses (b) and (c) of claim 4 and do not directly discuss a potential utility for the product described by clause (a) of claim 4.

Second, neither the arguments of Paper No. 12 nor any paragraph of the Declaration of Paper No. 11, contest or contradict the finding of Paper No. 10, mailed September 23, 2002, that no prior art polypeptide having a known or proposed function shares any significant degree of amino acid homology with the polypeptide of SEQ ID NO:6. Indeed, SEQ ID NO:6 shares less than 10% sequence identity with prior art proteins for which a function has at least been proposed. Consequently, the putative association that the Declaration reports in paragraphs 6(e) - 6(g), to have been made in the absent article of Thompson et al. is unavailable on the present record: No interaction can be attributed to a polypeptide of SEQ ID NO:6, or a mRNA transcript having a nucleic acid sequence corresponding to SEQ ID NO:4 present in a nerve cell, with any other polypeptide contemporaneously expressed by, or transcript present in, human nerve cells. While a set of neurotransmitter-processing enzymes, and their mRNA transcripts, previously recited in the canceled claim 1, that Applicant desires to link to the polypeptide of SEQ ID NO:6 or a nucleic acid sequence corresponding to SEQ ID NO:4 are reported to have some degree of association with some medical conditions involving the human central nervous system, Applicant's arguments of Paper No. 12, and the Declaration's statements, contemplate a twice-removed "guilt-by-association analysis": guilt-by-association of a transcript encoding a product with no known function in 12 cDNA libraries, see page 24 of the specification, to two products guilty-by-association with certain disorders.

Third, neither the gene transcribed as a nucleic acid sequence corresponding to SEQ ID NO:4 herein, nor its encoded product of SEQ ID NO:6 herein, are shown to have any

association with either upregulation of neurotransmitter gene expression or downregulation of such gene expression, nor an association with modulation of cellular response to any neurotransmitter or processing any neurotransmitter, nor association with any other nerve cell activity. This is because there is no negative control in the specification that might indicate that levels of expression of products of SEQ ID NO:4 and/or SEQ ID NO:6 differ in normal central nervous system neurons from their expression levels in, e.g., neuronal precursor cells or in neurons that contribute to a medical condition or disease as indicated in paragraphs 5(b) and (d) in the Declaration for the absent article's analysis of "guilt-by-association". Thus the specification when combined with the Declaration is not seen to establish any specific and substantial association, or prospective utility, for the elected subject matter of a polynucleotide having the nucleotide sequence of SEQ ID NO:4 or its complement or for the elected polypeptide having the amino acid sequence of SEQ ID NO:6, particularly in the absence of the referenced article.

A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The specification fails to indicate in its disclosure of pages 20-25 that the gene 2823339 transcript, or product, are differentially expressed in glial cells or paraganglionic neurons in a normal state versus diseased or otherwise altered states and also fails to indicate whether or not the transcript or product are also expressed in other nervous tissue elements. Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific utility that is substantial. The rejection of record is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 4-8 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a **specific** asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 2 and 4-8 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection differs from the rejection stated in Paper No. 10 because it addresses, in part, the amendments of Paper No. 12 to clause (d) of claim 2 and to clause (c) of claim 4. This communication is not made final because the rejection also addresses clause (b) of claim 2, thus is not necessitated by Applicant's amendments and could have been made in Paper No. 10. The specification fails to exemplify or describe the design, preparation, or isolation of nucleic acid sequence products of the amended clause (d) of claim 2 that diverge in their coding capacity from the elected nucleic acid sequence of SEQ ID NO:4. Clauses (b) and (c) of claim 2 are not subject to this rejection because one skilled in the relevant art would consider that disclosure of SEQ ID NO:4 herein constitutes an inherent disclosure of the design of isocoding nucleic acid sequences and their complements. The specification also fails to exemplify or describe the design, preparation, or isolation of polypeptide products of clause (b) and the amended clause (c) of claim 4 that diverge in their amino acid sequence from that set forth in SEQ ID NO:4. Claims 5-8 are subject to this rejection because they depend from either of claims 2 or 4, thus incorporate subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention at the time the application was filed. "While one does not need to have carried out one's

invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993).

The specification nowhere identifies any specific structural characteristic of the polypeptide having the amino acid sequence of SEQ ID NO:6, nor does it provide any informational characteristic of a nucleic acid encoding the amino acid sequence of SEQ ID NO:6, that would permitting a correlation between either of these products and any of the divergent products statistically described in the amendments to clause (d) of claim 2 and to clause (c) of claim 4 of Paper No. 12. Neither does the specification identify further structural characteristics of any polypeptide of clause (b) of claim 4 that comprises six contiguous amino acids of the amino acid sequence of SEQ ID NO:6 other than the polypeptide having the amino acid sequence of SEQ ID NO:6. The Court of Appeals for the Federal Circuit held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of claimed, divergent, products to provide the public with identifying "characteristics [that could] sufficiently" demonstrate to skilled artisans in the relevant field of molecular biology that Applicant possessed the claimed subject matter at the time the priority document for this application was filed on September 1, 1998. *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The treatment in the specification of the subject matters of clause (d) of claim 2 and of clauses (b) and (c) of claim 4 is entirely prospective where

skilled artisans in the relevant field of molecular biology could not predict the ways in which structures of claimed products differ from structures of the disclosed products. Deleting claim 2's clause (d), and claim 4's clauses (b) and (c), will avoid this rejection.

Claims 2 and 4-8 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for designing a nucleic acid sequence encoding the polypeptide having the amino acid sequence set forth in SEQ ID NO:6, and for preparing the encoded polypeptide,

does not reasonably provide enablement for designing or preparing a nucleic acid sequence encoding a polypeptide having an amino acid sequence differing from that set forth in SEQ ID NO:6 or for preparing a polypeptide having an amino acid sequence differing from that set forth in SEQ ID NO:6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection differs from the rejection stated in Paper No. 10 where it addresses, in part, amendments to clause (d) of claim 2 and to clause (c) of claim 4 of Paper No. 12. This communication is not made final where the rejection also addresses clause (b) of claim 2, is not necessitated by Applicant's amendments, and could have been made in Paper No. 10. With entry of the amendments of Paper No. 12, claims 2 and 4 now contemplate, in part, arbitrary alterations of the amino acid sequence of SEQ ID NO:6, and corresponding codon alterations of a nucleic acid sequence, such as SEQ ID NO:4, encoding the amino acid sequence of SEQ ID NO:6, at as many as ten of the amino acid positions therein without any teaching suggesting where, and how, the amino acid sequence, or encoding nucleic acid sequence might be altered. Clause (b) of claim 4 additionally contemplates arbitrary alteration, e.g., the removal, of up to 97% of the amino acid sequence of SEQ ID NO:6 where the remaining 3% of the amino acid sequence may be any hexapeptide that occurs anywhere in SEQ ID NO:6. There is no basis in the specification for either the lesser or the greater degree of amino acid sequence alteration, or corresponding codon alteration in an encoding nucleic acid sequence because neither the prior art of record nor Applicant's specification can identify, taken together, any function of the polypeptide SEQ ID NO:6, thus one of ordinary skill in the art seeking to prepare any of the myriad species

of polypeptide, or encoding polynucleotide, embraced by the scope of clauses (b) and (c) of claim 4, or the scope of clause (d) of claim 2, could not determine what to keep, or what and where to discard or alter, in the amino acid sequence. The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The Federal Circuit has considered whether definitional statements, such as statistical descriptions of identity, might enable a claim scope argued to extend beyond a disclosed gene product having its native amino acid sequence to embrace another, variant, gene product encoded by an altered DNA sequence. *Genentech, Inc. v. The Wellcome Found. Ltd.*, 29 F.3d 1555, 31 USPQ2d 1161 (Fed. Cir. 1994). The court held that

only a narrow structural and functional definition was enabling because the sweeping definitions of scope in the patent specification could not reasonably have been relied upon by the PTO in issuing the patent. *Genentech*, 29 F.3d 15 at 1564-65, 31 USPQ2d at 1168. The present specification can provides no basis whatsoever for a functional definition of the disclosed product and, applying the "*Forman*" factors discussed in *Wands*, *supra*, to Applicant's disclosure, it is apparent that:

a) the specification lacks any specific guidance for altering in any way the polypeptide having the amino acid sequence of SEQ ID NO:6,

b) the specification lacks working examples wherein a polypeptide having the amino acid sequence of SEQ ID NO:6, or its encoding nucleic acid sequence is altered in any way,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such formulation or administration, and,

d) unpredictability exists in the art where no similar polypeptide has been identified nor a biological function determined for distantly-related polypeptides.

This rejection may be avoided as to all elected claims by deleting clause (d) of claim 2 and clauses (b) and (c) of claim 4.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct FAX telephone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
March 4, 2003